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Supplementary appendix

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Supplement to: Ader F, Bouscambert-Duchamp M, Hites M, et al. Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): a phase 3, randomised, controlled, open-label trial. *Lancet Infect Dis* 2021; published online Sept 14. http://dx.doi.org/10.1016/https://doi.org/10.1016/S1473-3099(21)00485-0.

Supplementary Appendix

Remdesivir plus standard of care versus standard of care alone for the treatment of patients admitted to hospital with COVID-19 (DisCoVeRy): a phase 3, randomised, controlled, open-label trial

by Ader, F. et al.

Supplementary Methods – Virological Methods

NP swabs were collected through validated devices containing flocked swabs and virus transport medium. Respiratory samples were collected in sterile containers and were sent, as swabs, to the laboratory to be processed within 24 hours after sampling for SARS-CoV-2 detection, blind from allocated treatment. Each sample was then sent after freezing, to the National Centre for Viral Respiratory Infections (Hospices Civils de Lyon, France) for the determination of the normalised viral load. The analysis of the NP swab was performed blinded to treatment arm. RNA extraction was performed on the EMAG® platform (bioMerieux, Marcy-l'Étoile, France), using manufacturer's instructions. RNA was extracted from 200 µL of sample eluted in 50 µL of elution buffer. Then, SARS-CoV-2 viral load was measured by quantitative RT-PCR using the RT-PCR RdRp-IP4 developed by the French National Centre for Viral Respiratory Infections (Institut Pasteur, Paris) widely used in French laboratories at the beginning of the pandemic. The amplification protocol was developed for viral quantification using QuantStudio 5 *rt*PCR Systems (Thermo Fisher Scientific, Waltham, Massachusetts, USA). This RT-PCR targets the RdRp gene and is one of the most sensitive methods available [1] . SARS-COV-2 viral loads were measured according to a scale of calibrated in-house plasmids, harbouring the RdRp target and developed specifically for this quantification. The 10-fold diluted calibrated plasmid ranges from 5.10^2 to 5.10^6 copies/5 µL. The strict validation criteria applied to each PCR allowed for a reproductible quantification run after run. The quality of NP swabs was checked using the CELL Control r-gene® kit (Argene_BioMérieux, Marcy-l'Étoile, France) targeting the human gene HPRT-1. This kit is provided with a quantified plasmid for cellular quantification. If cell quantification was below 500 cells/5µL, the sample was considered of poor quality for viral load to be measured. To homogenise the viral loads determinations between participants and sampling times, we computed a normalised SARS-CoV-2 viral load by dividing the viral load measured in the sample by the number of cells measured, and expressed it in $\log_{10}$ of RNA copies per 10 000 cells. The limit of detection (LoD) of RT-PCR for the viral load was 4 copies / reaction, which corresponds to a limit of detection for normalised viral loads of 1 $\log_{10}$ copies/100 000 cells. We estimated the LoD using a probit analysis by analysing dilutions of a quantified cell culture supernatants. Probit analysis consists of describing the relationship between the probability of detection and concentration using a cumulative probability curve. For each dilution, the ratio (the hit rate) is computed as the number of replicates with a detected outcome per the total number of replicates tested. These hit rates are converted mathematically into cumulative normal probability units (probits) and fitted using a regression model *vs.* their respective concentrations. The LoD is defined as the lowest amount of viral genome that can be detected with a 95% hit rate. In the study, all viral loads strictly under 1 $\log_{10}$ copies/100 000 cells were considered under the LoD and were reported in the e-CRF as a negative result. If a rebound in viral excretion was observed, the sample was retested for confirmation.

Supplementary References

1 Etievant S, Bal A, Escuret V, *et al.* Performance Assessment of SARS-CoV-2 PCR Assays Developed by WHO Referral Laboratories. *J Clin Med* 2020; **9**. http://www.ncbi.nlm.nih.gov/pubmed/32560044.

Supplementary Table S1. Baseline characteristics of participants included in the intention to treat population of the DisCoVeRy trial, overall and according to randomization arm and to disease severity at randomization.
NPS, Nasopharyngeal swabs. * denotes variables with missing data.

	Moderate			Severe		
	Overall (N=504)	**Remdesivir (N=253)**	**Control (N=251)**	**Overall (N=328)**	**Remdesivir (N=161)**	**Control (N=167)**
Median age — yr [IQR]	63 [53; 73]	62 [54; 73]	64 [52; 72]	65 [56; 72]	64 [56; 73]	65 [56; 72]
Male sex — no. (%)	336 (66.7%)	165 (65.2%)	171 (68.1%)	243 (74.1%)	126 (78.3%)	117 (70.1%)
Ethnicity* — no. (%)						
- Caucasian	286 (63.4%)	137 (60.6%)	149 (66.2%)	213 (78.0%)	107 (79.9%)	106 (76.3%)
- North African	70 (15.5%)	34 (15.0%)	36 (16.0%)	40 (14.7%)	15 (11.2%)	25 (18.0%)
- Sub-Saharan African	37 (8.2%)	25 (11.1%)	12 (5.3%)	10 (3.7%)	5 (3.7%)	5 (3.6%)
- Other	58 (12.9%)	30 (13.3%)	28 (12.4%)	10 (3.7%)	7 (5.2%)	3 (2.2%)
Number of coexisting conditions* — no. (%)						
- 0	133 (26.6%)	65 (26.0%)	68 (27.2%)	86 (26.5%)	44 (27.8%)	42 (25.3%)
- 1	175 (35.0%)	89 (35.6%)	86 (34.4%)	101 (31.2%)	53 (33.5%)	48 (28.9%)
- 2	116 (23.2%)	65 (26.0%)	51 (20.4%)	78 (24.1%)	32 (20.3%)	46 (27.7%)
- >2	76 (15.2%)	31 (12.4%)	45 (18.0%)	59 (18.2%)	29 (18.4%)	30 (18.1%)
Coexisting condition* — no. (%)						
- Obesity	150 (30.4%)	77 (31.4%)	73 (29.4%)	128 (39.6%)	61 (38.9%)	67 (40.4%)
- Chronic cardiac disease	138 (27.6%)	74 (29.6%)	64 (25.6%)	91 (28.2%)	37 (23.6%)	54 (32.5%)
- Diabetes mellitus	132 (26.4%)	66 (26.4%)	66 (26.4%)	85 (26.2%)	38 (24.1%)	47 (28.3%)
- Chronic pulmonary disease	93 (18.6%)	44 (17.6%)	49 (19.6%)	53 (16.4%)	27 (17.2%)	26 (15.7%)
- Chronic kidney disease (stage 1 to 3)	28 (5.6%)	11 (4.4%)	17 (6.8%)	23 (7.1%)	8 (5.1%)	15 (9.0%)
- Auto-inflammatory disease	26 (5.2%)	11 (4.4%)	15 (6.0%)	15 (4.6%)	6 (3.8%)	9 (5.4%)
- Malignant hemopathy	16 (3.5%)	5 (2.2%)	11 (4.8%)	19 (6.7%)	11 (8.0%)	8 (5.6%)
- Chronic neurological disorder (including dementia)	21 (4.2%)	9 (3.6%)	12 (4.8%)	13 (4.0%)	9 (5.7%)	4 (2.4%)
- Mild liver disease	19 (3.8%)	9 (3.6%)	10 (4.0%)	11 (3.4%)	6 (3.8%)	5 (3.0%)
- Active malignant neoplasm	22 (4.4%)	10 (4.0%)	12 (4.8%)	6 (1.9%)	3 (1.9%)	3 (1.8%)
- Transplantation	5 (1.0%)	1 (0.4%)	4 (1.6%)	6 (1.9%)	1 (0.6%)	5 (3.0%)
- Asplenia	3 (0.6%)	0 (0.0%)	3 (1.2%)	1 (0.3%)	1 (0.6%)	0 (0.0%)
- AIDS / HIV not on HAART	2 (0.4%)	0 (0.0%)	2 (0.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
- Smoking status (current or former)	85 (17.8%)	46 (19.4%)	39 (16.2%)	56 (18.2%)	27 (17.8%)	29 (18.7%)
- Smoking status (current)	19 (4.0%)	10 (4.2%)	9 (3.7%)	13 (4.2%)	5 (3.3%)	8 (5.2%)

	Moderate			Severe		
	Overall (N=504)	**Remdesivir (N=253)**	**Control (N=251)**	**Overall (N=328)**	**Remdesivir (N=161)**	**Control (N=167)**
Median time from symptoms onset to randomization* — days [IQR]	8.0 [6.0; 11.0]	9.0 [6.0; 11.0]	8.0 [6.0; 11.0]	9.0 [7.0; 12.0]	9.0 [7.0; 11.0]	10.0 [7.0; 12.0]
Severity of COVID-19 at randomization — no. (%)						
- Moderate	504 (100.0%)	253 (100.0%)	251 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
- Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	328 (100.0%)	161 (100.0%)	167 (100.0%)
Ventilatory support at randomization — no. (%)						
- Room air	12 (2.4%)	6 (2.4%)	6 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
- Oxygen support (Nasal cannula, face mask)	492 (97.6%)	247 (97.6%)	245 (97.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
- High Flow Oxygen device (e.g. optiflow)	0 (0.0%)	0 (0.0%)	0 (0.0%)	148 (45.1%)	71 (44.1%)	77 (46.1%)
- Non-Invasive ventilation	0 (0.0%)	0 (0.0%)	0 (0.0%)	31 (9.5%)	15 (9.3%)	16 (9.6%)
- Invasive Mechanical Ventilation	0 (0.0%)	0 (0.0%)	0 (0.0%)	147 (44.8%)	75 (46.6%)	72 (43.1%)
- ECMO	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.6%)	0 (0.0%)	2 (1.2%)
NEWS-2* — no. (%)	7.0 [6.0-9.0]	7.0 [5.0-9.0]	7.0 [6.0-9.0]	10.0 [9.0-13.0]	10.0 [9.0-13.0]	10.0 [9.0-12.5]
7-point ordinal scale at baseline — no. (%)						
3. Hospitalized, not requiring supplemental oxygen	16 (3.2%)	8 (3.2%)	8 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
4. Hospitalized, requiring supplemental oxygen	464 (92.1%)	233 (92.1%)	231 (92.0%)	21 (6.4%)	8 (5.0%)	13 (7.8%)
5. Hospitalized, on non-invasive ventilation or high flow oxygen devices	22 (4.4%)	11 (4.3%)	11 (4.4%)	161 (49.1%)	79 (49.1%)	82 (49.1%)
6. Hospitalized, on invasive mechanical ventilation or ECMO	2 (0.4%)	1 (0.4%)	1 (0.4%)	146 (44.5%)	74 (46.0%)	72 (43.1%)
Randomization site* — no. (%)						
- ICU	51 (10.2%)	29 (11.6%)	22 (8.8%)	314 (96.6%)	153 (96.2%)	161 (97.0%)
- Conventional unit	449 (89.8%)	221 (88.4%)	228 (91.2%)	11 (3.4%)	6 (3.8%)	5 (3.0%)
Median viral load on NPS at baseline* – $\log_{10}$ cp/10,000 cells [IQR]	3.0 [1.7; 4.4]	3.2 [1.7; 4.5]	2.8 [1.8; 4.3]	3.5 [1.9; 4.8]	3.4 [1.8; 4.5]	3.8 [2.1; 5.0]
Biological data at baseline* – median [IQR]						
- Minimal lymphocyte count (10^9/L)	0.9 [0.7; 1.3]	0.9 [0.7; 1.2]	0.9 [0.7; 1.4]	0.7 [0.5; 0.9]	0.7 [0.5; 0.9]	0.7 [0.5; 0.9]
- Maximal neutrophil count (10^9/L)	4.7 [3.3; 7.4]	4.8 [3.3; 7.8]	4.7 [3.2; 6.8]	7.1 [5.1; 9.9]	7.1 [5.8; 9.7]	7.0 [4.6; 10.0]
- Maximal platelet count (10^9/L)	208.5 [162.0; 286.0]	209.5 [168.0; 295.0]	204.5 [159.0; 284.0]	244.0 [183.0; 306.5]	243.0 [179.0; 320.0]	244.0 [187.0; 301.0]
- Maximal urea (mmol/L)	6.0 [4.0; 8.0]	6.0 [4.0; 8.0]	6.0 [4.0; 8.0]	8.0 [6.0; 11.0]	8.0 [6.0; 11.0]	7.5 [5.0; 11.0]
- Maximal creatininemia (µmol/L)	75.0 [61.0; 91.0]	74.0 [60.0; 92.0]	75.0 [61.0; 91.0]	74.0 [61.0; 98.0]	73.0 [60.0; 97.0]	75.5 [61.0; 99.0]
- Maximal AST / SGOT (U/L)	44.0 [32.0; 63.0]	44.0 [32.0; 67.0]	44.0 [31.0; 60.0]	49.0 [35.0; 71.0]	48.0 [35.0; 68.0]	50.0 [36.0; 73.0]
- Maximal ALT / SGPT (U/L)	36.0 [23.0; 59.0]	36.0 [24.0; 55.0]	37.0 [23.0; 59.0]	38.0 [23.0; 61.0]	35.0 [23.0; 53.0]	40.0 [24.0; 65.0]
- Maximal Total Bilirubin (µmol/L)	8.6 [6.0; 12.0]	8.3 [6.0; 12.0]	8.7 [6.0; 12.0]	9.0 [6.0; 13.0]	8.8 [6.0; 12.0]	9.0 [6.0; 13.2]

	Moderate			Severe		
	Overall (N=504)	**Remdesivir (N=253)**	**Control (N=251)**	**Overall (N=328)**	**Remdesivir (N=161)**	**Control (N=167)**
- Maximal International Normalized Ratio	1.1 [1.0; 1.2]	1.1 [1.0; 1.2]	1.1 [1.0; 1.2]	1.1 [1.0; 1.2]	1.1 [1.0; 1.2]	1.1 [1.1; 1.3]
- Maximal C-Reactive Protein (mg/L)	92.0 [49.0; 151.0]	89.5 [49.5; 143.0]	96.0 [49.0; 157.0]	126.5 [78.0; 195.5]	122.0 [74.0; 183.0]	130.0 [80.0; 205.0]
- Maximal D-Dimers (µg/L)	828.0 [540.0; 1300.0]	805.0 [500.0; 1217.0]	913.0 [570.0; 1491.5]	1155.0 [620.0; 2355.0]	1208.0 [711.0; 2345.0]	1080.0 [620.0; 2355.0]
- Maximal Procalcitonin (g/mL)	0.2 [0.1; 0.4]	0.2 [0.1; 0.4]	0.2 [0.1; 0.4]	0.3 [0.2; 1.2]	0.3 [0.1; 1.0]	0.4 [0.2; 1.6]
- Maximal Ferritin max - mg/L)	666.5 [339.0; 1404.5]	726.5 [401.0; 1435.0]	614.0 [116.0; 1400.0]	913.0 [418.0; 1804.0]	1088.5 [546.5; 2027.0]	864.0 [376.0; 1763.0]

Supplementary Table S2. Concomitant treatments received during the study course in the patients included in the intention-to-treat population of the DisCoVeRy trial, overall, according to randomization arm and to disease severity at randomization.

	All patients			Moderate			Severe		
	Overall (N=832)	**Remdesivir (N=414)**	**Control (N=418)**	**Overall (N=504)**	**Remdesivir (N=253)**	**Control (N=251)**	**Overall (N=328)**	**Remdesivir (N=161)**	**Control (N=167)**
Corticosteroids (general route) — no. (%)	333 (40.0%)	164 (39.6%)	169 (40.4%)	201 (39.9%)	96 (37.9%)	105 (41.8%)	132 (40.2%)	68 (42.2%)	64 (38.3%)
- Dexamethasone	271 (32.6%)	139 (33.6%)	132 (31.6%)	166 (32.9%)	86 (34.0%)	80 (31.9%)	105 (32.0%)	53 (32.9%)	52 (31.1%)
- Hydrocortisone	24 (2.9%)	10 (2.4%)	14 (3.3%)	8 (1.6%)	4 (1.6%)	4 (1.6%)	16 (4.9%)	6 (3.7%)	10 (6.0%)
- Methylprednisolone	47 (5.6%)	23 (5.6%)	24 (5.7%)	26 (5.2%)	11 (4.3%)	15 (6.0%)	21 (6.4%)	12 (7.5%)	9 (5.4%)
Corticosteroids (inhaled route) — no. (%)	62 (7.5%)	27 (6.5%)	35 (8.4%)	43 (8.5%)	20 (7.9%)	23 (9.2%)	19 (5.8%)	7 (4.3%)	12 (7.2%)
Interleukin-6 inhibitors — no. (%)	7 (0.8%)	5 (1.2%)	2 (0.5%)	5 (1.0%)	4 (1.6%)	1 (0.4%)	2 (0.6%)	1 (0.6%)	1 (0.6%)
- Tocilizumab	7 (0.8%)	5 (1.2%)	2 (0.5%)	5 (1.0%)	4 (1.6%)	1 (0.4%)	2 (0.6%)	1 (0.6%)	1 (0.6%)
Interleukin-1 inhibitors — no. (%)	4 (0.5%)	3 (0.7%)	1 (0.2%)	3 (0.6%)	2 (0.8%)	1 (0.4%)	1 (0.3%)	1 (0.6%)	0 (0.0%)
Angiotensin-receptor blockers — no. (%)	75 (9.0%)	33 (8.0%)	42 (10.0%)	52 (10.3%)	24 (9.5%)	28 (11.2%)	23 (7.0%)	9 (5.6%)	14 (8.4%)
Antibiotics — no. (%)	344 (41.3%)	178 (43.0%)	166 (39.7%)	193 (38.3%)	96 (37.9%)	97 (38.6%)	151 (46.0%)	82 (50.9%)	69 (41.3%)
- Azithromycin	15 (1.8%)	11 (2.7%)	4 (1.0%)	14 (2.8%)	10 (4.0%)	4 (1.6%)	1 (0.3%)	1 (0.6%)	0 (0.0%)
Anticoagulants — no. (%)	436 (52.4%)	212 (51.2%)	224 (53.6%)	266 (52.8%)	130 (51.4%)	136 (54.2%)	170 (51.8%)	82 (50.9%)	88 (52.7%)
Parenteral or enteral nutrition — no. (%)	257 (30.9%)	125 (30.2%)	132 (31.6%)	68 (13.5%)	33 (13.0%)	35 (13.9%)	189 (57.6%)	92 (57.1%)	97 (58.1%)
Vasopressors — no. (%)	231 (27.8%)	107 (25.8%)	124 (29.7%)	50 (9.9%)	25 (9.9%)	25 (10.0%)	181 (55.2%)	82 (50.9%)	99 (59.3%)
Extra-renal replacement/hemofiltration — no. (%)	34 (4.1%)	10 (2.4%)	24 (5.7%)	8 (1.6%)	3 (1.2%)	5 (2.0%)	26 (7.9%)	7 (4.3%)	19 (11.4%)
Neuromuscular blocking agents — no. (%)	210 (25.2%)	97 (23.4%)	113 (27.0%)	47 (9.3%)	23 (9.1%)	24 (9.6%)	163 (49.7%)	74 (46.0%)	89 (53.3%)
Inhaled nitric oxide — no. (%)	32 (3.8%)	15 (3.6%)	17 (4.1%)	8 (1.6%)	4 (1.6%)	4 (1.6%)	24 (7.3%)	11 (6.8%)	13 (7.8%)
Prone positioning — no. (%)	194 (23.3%)	95 (22.9%)	99 (23.7%)	43 (8.5%)	24 (9.5%)	19 (7.6%)	151 (46.0%)	71 (44.1%)	80 (47.9%)

Supplementary Table S3. Administration of corticosteroids by general route, before and after June, 30th 2020 in the intention-to-treat population of the DisCoVeRy trial, overall and according to randomization arm and to disease severity at randomization.

On June 30th, 2020, results from the RECOVERY trial reported the efficacy of dexamethasone in reducing mortality of patients hospitalized with COVID-19.

Corticosteroids (general route) — no. (%)	**All patients**			**Moderate**			**Severe**		
	Overall (N=832)	**Remdesivir (N=414)**	**Control (N=418)**	**Overall (N=504)**	**Remdesivir (N=253)**	**Control (N=251)**	**Overall (N=328)**	**Remdesivir (N=161)**	**Control (N=167)**
Patients randomized before June 30, 2020	80/298 (26.8%)	40/150 (26.7%)	40/148 (27.0%)	43/188 (22.9%)	21/94 (22.3%)	22/94 (23.4%)	37/110 (33.6%)	19/56 (33.9%)	18/54 (33.3%)
Patients randomized after June 30, 2020	253/534 (47.4%)	124/264 (47.0%)	129/270 (47.8%)	158/316 (50.0%)	75/159 (47.2%)	83/157 (52.9%)	95/218 (43.6%)	49/105 (46.7%)	46/113 (40.7%)

Supplementary Table S4. Secondary outcomes in the intention-to-treat population of the DisCoVeRy trial, overall, according to randomization arm and to severity at randomization.

Analyses were stratified on the disease severity at randomization and adjusted effect measures are reported in the table. ECMO, extracorporeal membrane oxygenation; OR, Odds-ratio; HR, Hazard ratio; LSMD, least-square mean difference. Estimates are reported with their 95% confidence interval.

	Overall (N=832)		**Moderate (N=504)**		**Severe (N=328)**		**Remdesivir vs. control Effect measure (95%CI)**
	Remdesivir (N=414)	**Control (N=418)**	**Remdesivir (N=253)**	**Control (N=251)**	**Remdesivir (N=161)**	**Control (N=167)**	
7-point ordinal scale at day 3 — no. (%)							OR=0.95 (0.72 to 1.26) [P=0.71]
3. Hospitalized, not requiring supplemental oxygen	23 (5.6%)	34 (8.1%)	23 (9.1%)	34 (13.5%)	0 (0.0%)	0 (0.0%)	
4. Hospitalized, requiring supplemental oxygen	186 (44.9%)	186 (44.5%)	178 (70.4%)	176 (70.1%)	8 (5.0%)	10 (6.0%)	
5. Hospitalized, on non-invasive ventilation or high flow oxygen devices	104 (25.1%)	78 (18.7%)	37 (14.6%)	25 (10.0%)	67 (41.6%)	53 (31.7%)	
6. Hospitalized, on invasive mechanical ventilation or ECMO	99 (23.9%)	117 (28.0%)	15 (5.9%)	16 (6.4%)	84 (52.2%)	101 (60.5%)	
7. Death	2 (0.5%)	3 (0.7%)	0 (0.0%)	0 (0.0%)	2 (1.2%)	3 (1.8%)	
7-point ordinal scale at day 5 — no. (%)							OR=1.03 (0.79 to 1.33) [P=0.84]
1. Not hospitalized, no limitations on activities	1 (0.2%)	5 (1.2%)	1 (0.4%)	5 (2.0%)	0 (0.0%)	0 (0.0%)	
2. Not hospitalized, limitation on activities	2 (0.5%)	14 (3.3%)	2 (0.8%)	14 (5.6%)	0 (0.0%)	0 (0.0%)	
3. Hospitalized, not requiring supplemental oxygen	71 (17.1%)	57 (13.6%)	65 (25.7%)	52 (20.7%)	6 (3.7%)	5 (3.0%)	
4. Hospitalized, requiring supplemental oxygen	154 (37.2%)	157 (37.6%)	133 (52.6%)	135 (53.8%)	21 (13.0%)	22 (13.2%)	
5. Hospitalized, on non-invasive ventilation or high flow oxygen devices	76 (18.4%)	55 (13.2%)	32 (12.6%)	24 (9.6%)	44 (27.3%)	31 (18.6%)	
6. Hospitalized, on invasive mechanical ventilation or ECMO	105 (25.4%)	122 (29.2%)	18 (7.1%)	19 (7.6%)	87 (54.0%)	103 (61.7%)	
7. Death	5 (1.2%)	8 (1.9%)	2 (0.8%)	2 (0.8%)	3 (1.9%)	6 (3.6%)	
7-point ordinal scale at day 8 — no. (%)							OR=0.91 (0.71 to 1.16) [P=0.43]
1. Not hospitalized, no limitations on activities	12 (2.9%)	24 (5.7%)	12 (4.7%)	24 (9.6%)	0 (0.0%)	0 (0.0%)	
2. Not hospitalized, limitation on activities	40 (9.7%)	57 (13.6%)	35 (13.8%)	52 (20.7%)	5 (3.1%)	5 (3.0%)	
3. Hospitalized, not requiring supplemental oxygen	82 (19.8%)	67 (16.0%)	70 (27.7%)	55 (21.9%)	12 (7.5%)	12 (7.2%)	
4. Hospitalized, requiring supplemental oxygen	134 (32.4%)	113 (27.0%)	98 (38.7%)	79 (31.5%)	36 (22.4%)	34 (20.4%)	
5. Hospitalized, on non-invasive ventilation or high flow oxygen devices	43 (10.4%)	34 (8.1%)	16 (6.3%)	15 (6.0%)	27 (16.8%)	19 (11.4%)	
6. Hospitalized, on invasive mechanical ventilation or ECMO	92 (22.2%)	110 (26.3%)	18 (7.1%)	21 (8.4%)	74 (46.0%)	89 (53.3%)	
7. Death	11 (2.7%)	13 (3.1%)	4 (1.6%)	5 (2.0%)	7 (4.3%)	8 (4.8%)	
7-point ordinal scale at day 11 — no. (%)							OR=0.93 (0.73 to 1.19) [P=0.58]
1. Not hospitalized, no limitations on activities	25 (6.0%)	40 (9.6%)	22 (8.7%)	35 (13.9%)	3 (1.9%)	5 (3.0%)	
2. Not hospitalized, limitation on activities	93 (22.5%)	108 (25.8%)	78 (30.8%)	94 (37.5%)	15 (9.3%)	14 (8.4%)	
3. Hospitalized, not requiring supplemental oxygen	79 (19.1%)	48 (11.5%)	62 (24.5%)	33 (13.1%)	17 (10.6%)	15 (9.0%)	
4. Hospitalized, requiring supplemental oxygen	97 (23.4%)	82 (19.6%)	62 (24.5%)	49 (19.5%)	35 (21.7%)	33 (19.8%)	

	Overall (N=832)		**Moderate (N=504)**		**Severe (N=328)**		**Remdesivir vs. control Effect measure (95%CI)**
	Remdesivir (N=414)	**Control (N=418)**	**Remdesivir (N=253)**	**Control (N=251)**	**Remdesivir (N=161)**	**Control (N=167)**	
5. Hospitalized, on non-invasive ventilation or high flow oxygen devices	27 (6.5%)	24 (5.7%)	6 (2.4%)	11 (4.4%)	21 (13.0%)	13 (7.8%)	
6. Hospitalized, on invasive mechanical ventilation or ECMO	78 (18.8%)	96 (23.0%)	17 (6.7%)	19 (7.6%)	61 (37.9%)	77 (46.1%)	
7. Death	15 (3.6%)	20 (4.8%)	6 (2.4%)	10 (4.0%)	9 (5.6%)	10 (6.0%)	
Time to improvement of 1 category of the 7-point ordinal scale within day 29 — median (IQR)	12 [8-24]	11 [7-26]	11 [8-20]	9 [6-15]	16 [10-29]	17 [10-29]	HR=1.09 (0.93 to 1.27) [P=0.28]
Change from baseline in the ordinal scale — median (IQR)							
– to day 3	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-0]	0 [0-1]	LSMD=-0.01 (-0.09 to 0.08) [P=0.90]
– to day 5	0 [0-0]	0 [0-0]	0 [-1-0]	0 [-1-0]	0 [0-0]	0 [0-1]	LSMD=0.00 (-0.12 to 0.12) [P=0.98]
– to day 8	0 [-1-0]	0 [-1-0]	0 [-1-0]	-1 [-2-0]	0 [-1-0]	0 [-1-1]	LSMD=0.05 (-0.12 to 0.22) [P=0.57]
– to day 11	-1 [-2-0]	-1 [-2-0]	-1 [-2-0]	-2 [-2-0]	0 [-2-0]	0 [-1-1]	LSMD=-0.02 (-0.22 to 0.19) [P=0.88]
– to day 15	-2 [-2-0]	-2 [-3-0]	-2 [-2-0]	-2 [-3-0]	-1 [-3-0]	0 [-3-1]	LSMD=-0.06 (-0.29 to 0.16) [P=0.60]
– to day 29	-2 [-3--1]	-2 [-3--1]	-2 [-3--1]	-2 [-3--1]	-3 [-4-0]	-2 [-3-0]	LSMD=-0.20 (-0.45 to 0.04) [P=0.11]
Change from baseline in NEWS2 — median (IQR)							
– to day 5	-1 [-3-1]	-1 [-3-1]	-1 [-4-1]	-1 [-4-1]	0 [-2-1]	0 [-2-2]	LSMD=-0.02 (-0.55 to 0.51) [P=0.95]
– to day 11	-2 [-5-1]	-2 [-4-1]	-3 [-5-0]	-2 [-5-0]	-1 [-4-2]	0 [-4-3]	LSMD=-0.36 (-1.04 to 0.32) [P=0.30]

	Overall (N=832)		**Moderate (N=504)**		**Severe (N=328)**		**Remdesivir vs. control Effect measure (95%CI)**
	Remdesivir (N=414)	**Control (N=418)**	**Remdesivir (N=253)**	**Control (N=251)**	**Remdesivir (N=161)**	**Control (N=167)**	
– to day 15	-3 [-6-0]	-2 [-5-0]	-4 [-6-0]	-4 [-6-0]	-2 [-6-2]	-1 [-4-3]	LSMD=-0.39 (-1.13 to 0.35) [P=0.31]
– to day 29	-4 [-7--1]	-4 [-7-0]	-4 [-7--1]	-4 [-7--2]	-4 [-8-0]	-3 [-7-2]	LSMD=-0.39 (-1.24 to 0.46) [P=0.37]

Supplementary Table S5. Proportion of patients with a detectable viral load, normalized viral load, change from baseline of normalized viral loads in the nasopharyngeal swabs at each sampling time in the intention-to-treat population of the DisCoVeRy trial, overall, according to randomization arm and to disease severity at randomization.

Analyses of detectable viral load were stratified on the disease severity at randomization and reported OR are adjusted on disease severity.
NP, nasopharyngeal; OR, odds ratio.

	All patients			**Moderate**			**Severe**			**Remdesivir vs. control Effect measure (95%CI)**
	Overall (N=832)	**Remdesivir (N=414)**	**Control (N=418)**	**Overall (N=504)**	**Remdesivir (N=253)**	**Control (N=251)**	**Overall (N=328)**	**Remdesivir (N=161)**	**Control (N=167)**	
Detectable viral load in NP swabs – n/N (%)										
- at baseline	372/426 (87.3%)	193/227 (85.0%)	179/199 (89.9%)	225/263 (85.6%)	117/139 (84.2%)	108/124 (87.1%)	147/163 (90.2%)	76/88 (86.4%)	71/75 (94.7%)	-
- at day 3	370/487 (76.0%)	197/252 (78.2%)	173/235 (73.6%)	223/304 (73.4%)	126/161 (78.3%)	97/143 (67.8%)	147/183 (80.3%)	71/91 (78.0%)	76/92 (82.6%)	OR=1.30 (0.86 to 1.97) [P=0.22]
- at day 5	306/467 (65.5%)	160/243 (65.8%)	146/224 (65.2%)	185/300 (61.7%)	99/158 (62.7%)	86/142 (60.6%)	121/167 (72.5%)	61/85 (71.8%)	60/82 (73.2%)	OR=1.04 (0.71 to 1.52) [P=0.85]
- at day 8	200/401 (49.9%)	105/212 (49.5%)	95/189 (50.3%)	117/237 (49.4%)	64/129 (49.6%)	53/108 (49.1%)	83/164 (50.6%)	41/83 (49.4%)	42/81 (51.9%)	OR=0.97 (0.66 to 1.44) [P=0.89]
- at day 11	126/290 (43.4%)	71/162 (43.8%)	55/128 (43.0%)	68/154 (44.2%)	41/89 (46.1%)	27/65 (41.5%)	58/136 (42.6%)	30/73 (41.1%)	28/63 (44.4%)	OR=1.03 (0.65 to 1.65) [P=0.89]
- at day 15	135/432 (31.3%)	62/217 (28.6%)	73/215 (34.0%)	86/282 (30.5%)	41/142 (28.9%)	45/140 (32.1%)	49/150 (32.7%)	21/75 (28.0%)	28/75 (37.3%)	OR=0.78 (0.52 to 1.17) [P=0.23]
- at day 29	33/349 (9.5%)	17/172 (9.9%)	16/177 (9.0%)	22/247 (8.9%)	11/121 (9.1%)	11/126 (8.7%)	11/102 (10.8%)	6/51 (11.8%)	5/51 (9.8%)	OR=1.10 (0.54 to 2.26) [P=0.79]
Median viral load in NP swabs, $\log_{10}$ cp/10,000 cells [IQR]										
- at baseline	3.2 [1.8; 4.5]	3.2 [1.7; 4.5]	3.2 [1.9; 4.5]	3.0 [1.7; 4.4]	3.2 [1.7; 4.5]	2.8 [1.8; 4.3]	3.5 [1.9; 4.8]	3.4 [1.8; 4.5]	3.8 [2.1; 5.0]	
- at day 3	2.3 [1.0; 3.7]	2.3 [1.2; 3.3]	2.2 [0.7; 3.8]	2.2 [0.7; 3.4]	2.3 [1.3; 3.1]	2.1 [0.7; 3.7]	2.5 [1.2; 3.9]	2.5 [1.2; 3.7]	2.5 [1.2; 4.4]	
- at day 5	1.7	1.6	1.7	1.5	1.5	1.6	1.9	1.7	2.3	

	[0.7; 3.1]	[0.7; 2.9]	[0.7; 3.5]	[0.7; 3.0]	[0.7; 2.9]	[0.7; 3.4]	[0.7; 3.2]	[0.7; 2.9]	[0.7; 3.8]	
- at day 8	0.7 [0.7; 2.2]	1.0 [0.7; 2.2]	0.7 [0.7; 2.3]	0.7 [0.7; 2.2]	1.0 [0.7; 2.2]	0.7 [0.7; 2.2]	0.9 [0.7; 2.3]	0.9 [0.7; 2.2]	0.9 [0.7; 2.5]	
- at day 11	0.7 [0.7; 2.0]	0.7 [0.7; 1.9]	0.7 [0.7; 2.1]	0.7 [0.7; 1.9]	0.7 [0.7; 1.8]	0.7 [0.7; 2.1]	0.7 [0.7; 2.0]	0.7 [0.7; 1.9]	0.7 [0.7; 2.1]	
- at day 15	0.7 [0.7; 1.2]	0.7 [0.7; 1.0]	0.7 [0.7; 1.2]	0.7 [0.7; 1.1]	0.7 [0.7; 1.0]	0.7 [0.7; 1.2]	0.7 [0.7; 1.3]	0.7 [0.7; 1.0]	0.7 [0.7; 1.5]	
Change from baseline of the normalized viral load in NP swabs, log_{10} cp/10,000 cells [IQR]										
- at day 3	-0.5 [-1.3; 0.0]	-0.5 [-1.4; 0.0]	-0.5 [-1.3; 0.0]	-0.5 [-1.2; 0.0]	-0.6 [-1.4; 0.0]	-0.5 [-1.2; 0.0]	-0.5 [-1.4; 0.3]	-0.4 [-1.4; 0.3]	-0.7 [-1.5; 0.1]	
- at day 5	-1.1 [-1.9; 0.0]	-1.1 [-1.9; 0.0]	-1.0 [-1.9; 0.0]	-1.0 [-1.8; 0.0]	-1.1 [-1.9; 0.0]	-0.9 [-1.8; 0.0]	-1.1 [-2.1; 0.0]	-1.1 [-2.0; 0.0]	-1.1 [-2.3; -0.4]	
- at day 8	-1.6 [-2.5; -0.4]	-1.6 [-2.6; -0.4]	-1.5 [-2.5; -0.3]	-1.5 [-2.4; -0.3]	-1.5 [-2.4; -0.4]	-1.5 [-2.5; -0.2]	-1.8 [-2.8; -0.4]	-1.8 [-2.9; -0.3]	-1.7 [-2.7; -0.4]	
- at day 11	-1.9 [-3.0; -0.5]	-2.0 [-3.0; -0.6]	-1.8 [-3.1; -0.5]	-1.9 [-2.8; -0.6]	-2.0 [-2.7; -0.6]	-1.6 [-3.0; -0.5]	-2.0 [-3.2; -0.5]	-2.2 [-3.2; -0.5]	-1.8 [-3.4; -0.5]	
- at day 15	-1.9 [-3.2; -0.8]	-2.0 [-3.2; -0.7]	-1.8 [-3.4; -0.9]	-1.7 [-3.1; -0.7]	-1.8 [-3.1; -0.5]	-1.6 [-3.2; -0.7]	-2.4 [-3.6; -1.3]	-2.4 [-3.6; -1.4]	-2.4 [-3.7; -1.2]	

Supplementary Table S6. Estimated intercepts and slopes of viral load decrease and difference of slopes between randomization arms, according to disease severity at randomization.
Analyses were stratified on the disease severity at randomization and reported effect measure is adjusted on disease severity at randomization. Intercepts and slopes are reported with their standard errors; difference of slopes is reported with its 95% confidence interval.

	Remdesivir		**Control**		**Remdesivir vs. control Effect measure (95%CI)**
	Moderate	Severe	Moderate	Severe	
Intercept, log_{10} cp/10,000 cells	2.84 (0.11)	3.01 (0.14)	3.02 (0.12)	3.18 (0.13)	-
Slope, log_{10} cp/10,000 cells/day	0.13 (0.01)	0.15 (0.01)	0.14 (0.01)	0.15 (0.01)	-0.004 (-0.03 to 0.02) [P=0.75]

Supplementary Table S7. Estimated intercepts and slopes of viral load decrease and difference of slopes between randomization arms, according to disease severity at randomization and to the duration of symptoms before randomization.
Intercepts and slopes are reported with their standard errors; differences of slopes are reported with their 95% confidence interval.

		Remdesivir	**Control**	**Remdesivir vs. control Effect measure (95%CI)**
Disease Severity				
Moderate	Intercept, log_{10} cp/10,000 cells	2.90 (0.13)	2.96 (0.14)	-
	Slope, log_{10} cp/10,000 cells/day	0.14 (0.01)	0.14 (0.01)	0.001 (-0.03 to 0.04) [P=0.95]
Severe	Intercept, log_{10} cp/10,000 cells	2.92 (0.16)	3.28 (0.16)	-
	Slope, log_{10} cp/10,000 cells/day	0.16 (0.02)	0.14 (0.02)	-0.014 (-0.06 to 0.03) [P=0.52]
Duration of symptoms prior to randomization				
≤ 7 days	Intercept, log_{10} cp/10,000 cells	3.33 (0.19)	3.76 (0.19)	-
	Slope, log_{10} cp/10,000 cells/day	0.18 (0.02)	0.17 (0.02)	-0.007 (-0.05 to 0.04) [P=0.75]
7 – 14 days	Intercept, log_{10} cp/10,000 cells	2.65 (0.12)	2.72 (0.12)	-
	Slope, log_{10} cp/10,000 cells/day	0.12 (0.01)	0.12 (0.01)	-0.006 (-0.04 to 0.03) [P=0.73]
>14 days	Intercept, log_{10} cp/10,000 cells	3.07 (0.43)	2.69 (0.37)	-
	Slope, log_{10} cp/10,000 cells/day	0.12 (0.04)	0.14 (0.05)	0.019 (-0.11 to 0.15) [P=0.78]

Supplementary Table S8. Plasma concentrations of remdesivir and its metabolite GS-441524, overall and according to disease severity at randomization, in remdesivir-treated participants from the DisCoVeRy trial.

		Overall	Moderate	Severe
Median post-infusion plasma concentration — ng/mL [IQR]				
at day 1	- n	52	38	14
	- remdesivir	2,790 [1,419; 4,935]	2,868 [760; 4,884]	2,617 [2,240; 5,180]
	- GS-441524	74 [51; 101]	72 [50; 98]	81 [59; 107]
Median trough plasma concentration — ng/mL [IQR]				
at day 2	- n	43	31	12
	- GS-441524	66 [51; 105]	67 [54; 109]	63 [50; 95.5]
at day 5	- n	30	19	11
	- GS-441524	61 [47; 94]	72 [57; 105]	53 [42; 69]
at day 8	- n	21	11	10
	- GS-441524	62 [44; 87]	70 [62; 121]	46.5 [37; 55]

Supplementary Table S9. Summary of adverse events according to treatment group in the modified intention-to-treat population of the DisCoVeRy trial, overall and according to randomization arm and to disease severity at randomization.

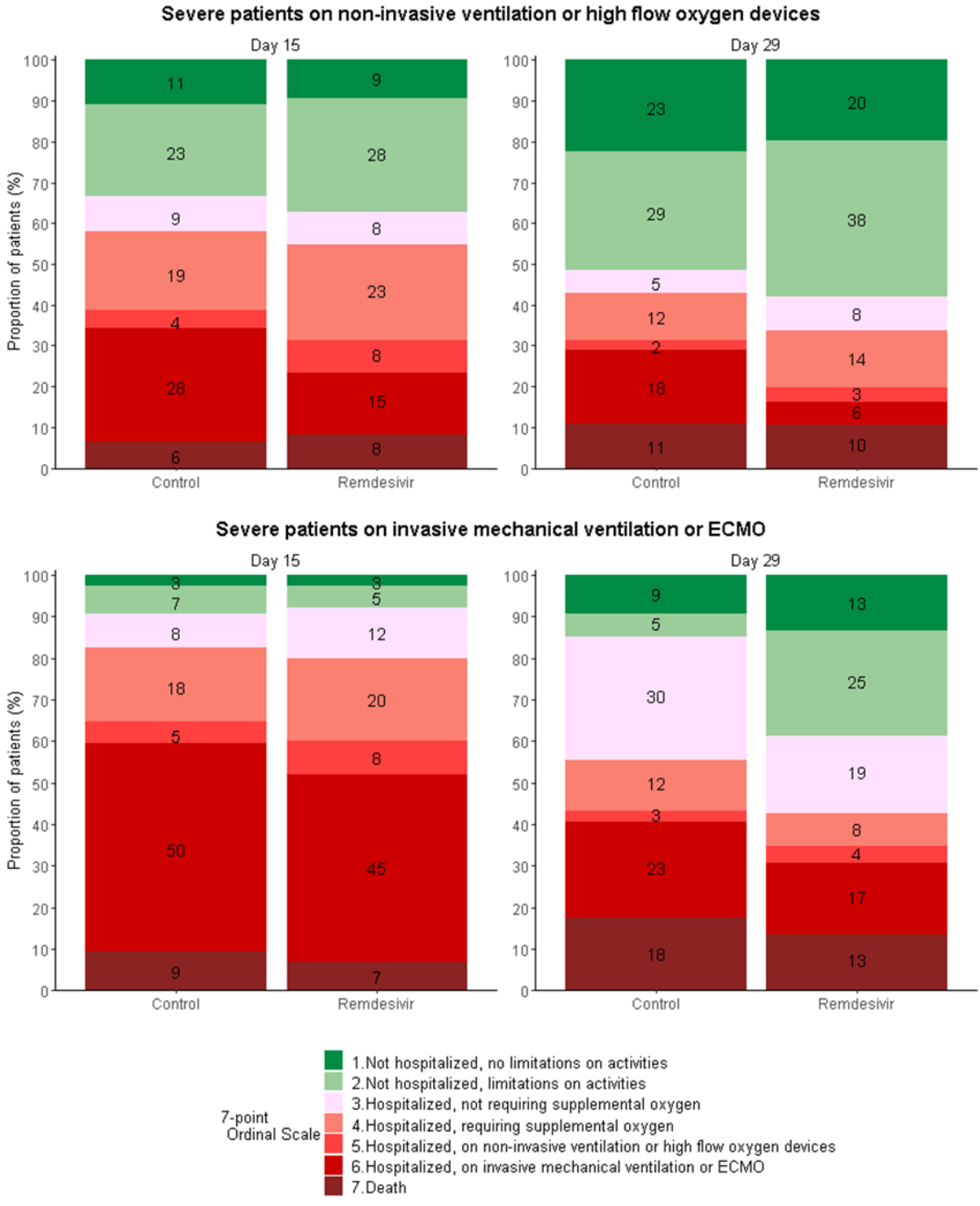
Numbers refer to number of patients (%). Some patients had more than a single AE. Analyses were performed on the modified Intention-to-treat population.

no (%)	Remdesivir (n=406)	Control (n=418)
Blood and lymphatic system disorders	10 (2%)	10 (2%)
- Anaemia	7 (2%)	8 (2%)
- Haemolytic anaemia	1 (0%)	0 (0%)
- Lymphopenia	1 (0%)	1 (0%)
- Thrombocytopenia	0 (0%)	1 (0%)
- Thrombocytosis	1 (0%)	0 (0%)
Cardiac disorders	21 (5%)	23 (6%)
- Acute coronary syndrome	0 (0%)	1 (0%)
- Arrhythmia	13 (3%)	6 (1%)
- Bradycardia	2 (0%)	2 (0%)
- Cardiac arrest	0 (0%)	4 (1%)
- Cardiac failure	1 (0%)	3 (1%)
- Congestive cardiomyopathy	0 (0%)	1 (0%)
- Left ventricular failure	0 (0%)	1 (0%)
- Myocardial ischaemia	1 (0%)	0 (0%)
- Myocarditis	0 (0%)	1 (0%)
- Tachycardia	4 (1%)	3 (1%)
- Ventricular arrhythmia	0 (0%)	1 (0%)
Gastrointestinal disorders	3 (1%)	7 (2%)
- Bezoar	0 (0%)	1 (0%)
- Faecaloma	1 (0%)	0 (0%)
- Gastrointestinal haemorrhage	0 (0%)	3 (1%)
- Gastrointestinal ulcer	0 (0%)	2 (0%)
- Intestinal ischaemia	1 (0%)	1 (0%)
- Oesophageal ulcer haemorrhage	1 (0%)	0 (0%)
General disorders and administration site conditions	5 (1%)	10 (2%)
- Chest pain	1 (0%)	0 (0%)
- General physical health deterioration	0 (0%)	1 (0%)
- Malaise	0 (0%)	1 (0%)
- Multiple organ dysfunction syndrom	4 (1%)	7 (2%)
- Oedema	0 (0%)	1 (0%)
Hepatobiliary disorders	1 (0%)	2 (0%)
- Cholangitis	0 (0%)	1 (0%)
- Hepatocellular injury	0 (0%)	1 (0%)
- Hepatorenal syndrome	1 (0%)	0 (0%)
Infections and infestations	21 (5%)	28 (7%)
- Aspergillus infection	0 (0%)	2 (0%)
- Bacterial infection	3 (1%)	3 (1%)
- Bronchitis	1 (0%)	0 (0%)
- Dengue fever	1 (0%)	0 (0%)
- Hepatitis viral	0 (0%)	1 (0%)
- Infection	1 (0%)	0 (0%)
- Pneumonia	8 (2%)	15 (4%)
- Sepsis	6 (1%)	6 (1%)
- Superinfection fungal	1 (0%)	0 (0%)
- Urinary tract infection	0 (0%)	1 (0%)
Injury, poisoning and procedural complications	16 (4%)	2 (0%)
- Mechanical ventilation complication	1 (0%)	0 (0%)

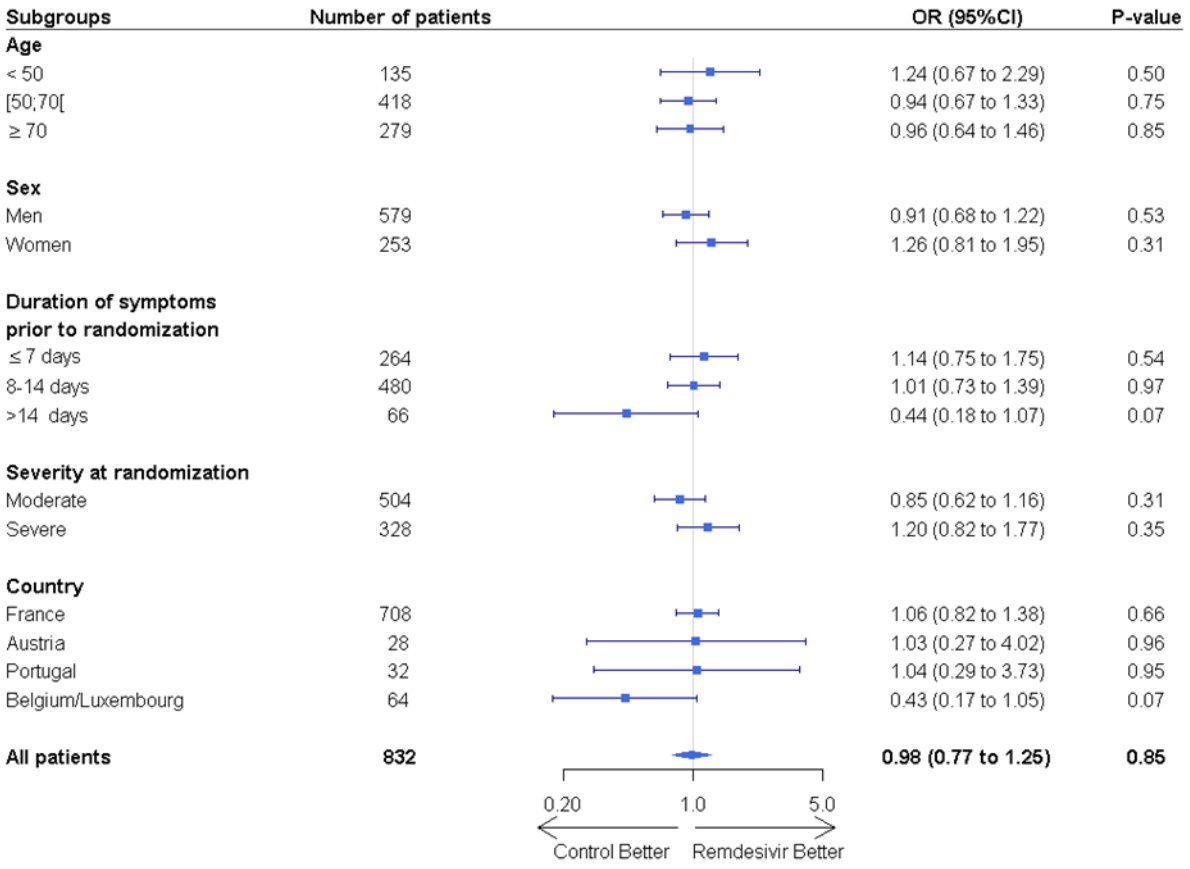
no (%)	Remdesivir (n=406)	Control (n=418)
- Overdose	1 (0%)	1 (0%)
- Product administration error	14 (3%)	0 (0%)
- Sedation complication	0 (0%)	1 (0%)
Investigations	20 (5%)	7 (2%)
- Aspartate aminotransferase increase	1 (0%)	0 (0%)
- Blood creatine phosphokinase increase	2 (0%)	1 (0%)
- Blood glucose increased	1 (0%)	0 (0%)
- Gamma-glutamyltransferase increase	1 (0%)	0 (0%)
- Glomerular filtration rate decrease	1 (0%)	0 (0%)
- Haemoglobin decreased	0 (0%)	1 (0%)
- Lipase increased	0 (0%)	1 (0%)
- Oxygen consumption increased	0 (0%)	1 (0%)
- Oxygen saturation decreased	1 (0%)	0 (0%)
- Serum creatinine increased	2 (0%)	0 (0%)
- Transaminases increased	11 (3%)	3 (1%)
Metabolism and nutrition disorders	9 (2%)	11 (3%)
- Alkalosis	1 (0%)	2 (0%)
- Decreased appetite	0 (0%)	1 (0%)
- Dehydration	1 (0%)	0 (0%)
- Hyperglycaemia	5 (1%)	4 (1%)
- Hyperkalaemia	0 (0%)	1 (0%)
- Hypernatremia	1 (0%)	0 (0%)
- Hypalbuminaemia	1 (0%)	1 (0%)
- Hyponatraemia	0 (0%)	1 (0%)
- Malnutrition	0 (0%)	1 (0%)
Neoplasms benign, malignant and unspecified	3 (1%)	4 (1%)
- Hepatic cancer	0 (0%)	1 (0%)
- Hepatocellular carcinoma	1 (0%)	0 (0%)
- Lung cancer metastatic	1 (0%)	0 (0%)
- Lung neoplasm malignant	0 (0%)	3 (1%)
- Malignant neoplasm progression	1 (0%)	0 (0%)
Nervous system disorders	6 (1%)	2 (0%)
- Acute haemorrhagic leukoencephalitis	1 (0%)	0 (0%)
- Cerebrovascular accident	2 (0%)	0 (0%)
- Encephalopathy	1 (0%)	0 (0%)
- Extrapyramidal disorder	1 (0%)	0 (0%)
- Hepatic encephalopathy	1 (0%)	0 (0%)
- Neuropathy peripheral	0 (0%)	1 (0%)
- Somnolence	0 (0%)	1 (0%)
Renal and urinary disorders	18 (4%)	23 (6%)
- Acute kidney injury	15 (4%)	18 (4%)
- Hepatorenal syndrome	0 (0%)	1 (0%)
- Renal failure	2 (0%)	3 (1%)
- Renal tubular disorder	1 (0%)	0 (0%)
- Urinary retention	0 (0%)	1 (0%)
Respiratory, thoracic and mediastinal disorders	90 (22%)	114 (27%)
- Acute respiratory distress syndrome	35 (9%)	37 (9%)
- Acute respiratory failure	30 (7%)	47 (11%)
- Dyspnoea	4 (1%)	3 (1%)
- Dyspnoea exertional	1 (0%)	0 (0%)
- Hypoxia	5 (1%)	4 (1%)
- Lung disorder	0 (0%)	1 (0%)
- Pleural effusion	4 (1%)	4 (1%)
- Pneumomediastinum	0 (0%)	1 (0%)
- Pneumothorax	2 (0%)	4 (1%)

no (%)	Remdesivir (n=406)	Control (n=418)
- Pulmonary embolism	8 (2%)	11 (3%)
- Pulmonary oedema	0 (0%)	1 (0%)
- Respiratory acidosis	1 (0%)	0 (0%)
- Respiratory alkalosis	0 (0%)	1 (0%)
Skin and subcutaneous tissue disorders	0 (0%)	2 (0%)
- Rash	0 (0%)	1 (0%)
- Subcutaneous emphysema	0 (0%)	1 (0%)
Vascular disorders	11 (3%)	4 (1%)
- Device related thrombosis	2 (0%)	0 (0%)
- Haemodynamic instability	1 (0%)	0 (0%)
- Hypertension	0 (0%)	1 (0%)
- Hypotension	2 (0%)	0 (0%)
- Orthostatic hypotension	1 (0%)	0 (0%)
- Shock	4 (1%)	1 (0%)
- Thrombosis	1 (0%)	2 (0%)

Supplementary Figure S1. Clinical status, as measured by the 7-point ordinal scale, at day 15 and day 29 in the intention-to-treat population of the DisCoVeRy trial, in severe patients stratified by absence (top) or presence (bottom) of invasive mechanical ventilation or ECMO at randomization.
Reported numbers refer to the proportion of patients with the corresponding level in each group.



Supplementary Figure S2. Forrest plot of subgroup analyses of the primary outcome in the intention-to-treat population of the DisCoVeRy trial.
The widths of the confidence intervals have not been adjusted for multiplicity and therefore cannot be used to infer treatment effects.

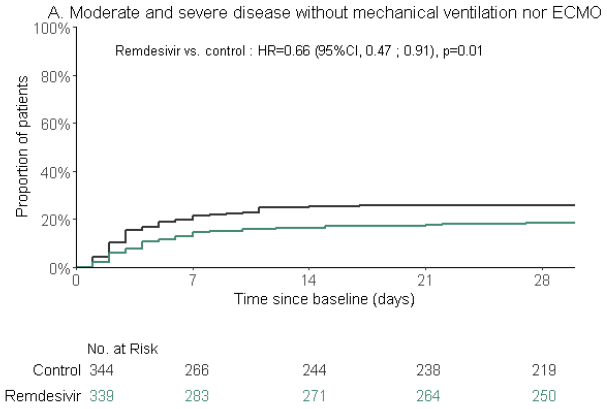


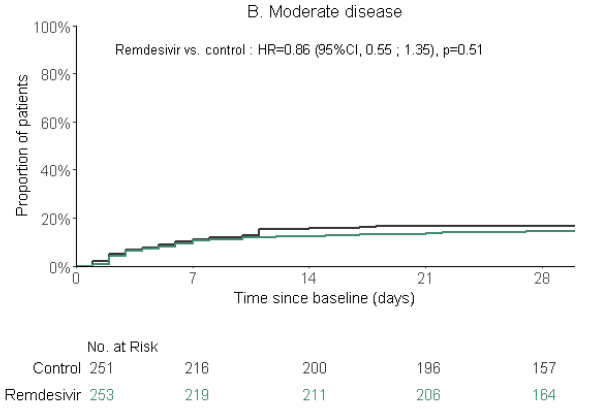
Supplementary Figure S3. Time to new mechanical ventilation, new ECMO or death between baseline and day 29 in the intention-to-treat population of the DisCoVeRy trial, according to disease severity at randomization in moderate and severe disease without ventilation or ECMO at randomization (panel A), in participants with moderate disease at randomization (panel B) and in participants with severe disease without ventilation or ECMO at randomization (panel C).

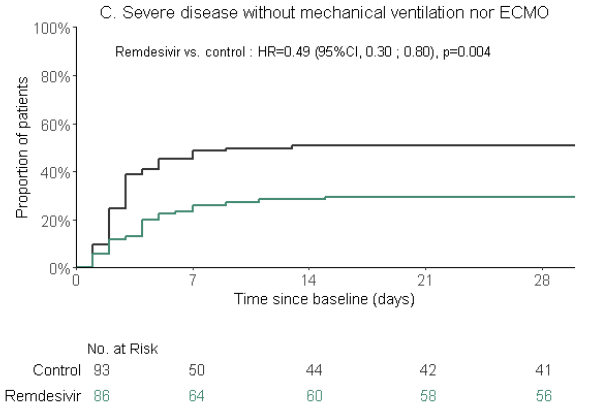
In the Panel A, analyses were stratified on the disease severity at randomization and reported hazard ratio is adjusted on disease severity at randomization.

In the panels B and C, we performed non-prespecified subgroup analyses according to the disease severity at baseline, and reported hazard ratios are specific to each disease severity subgroup.

Remdesivir (green line); control (black line). HR, Hazard ratio; 95%CI, 95% confidence interval.

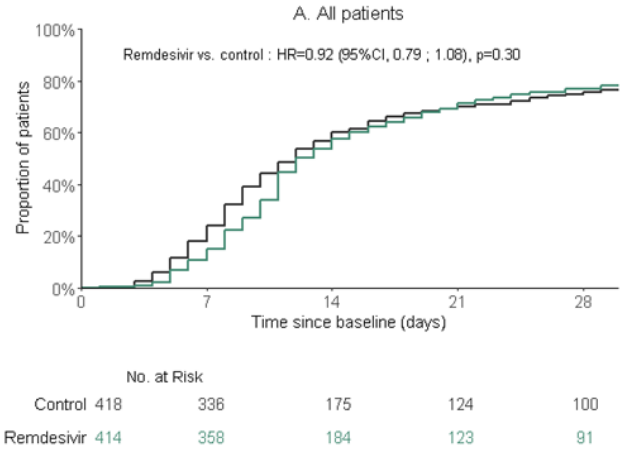


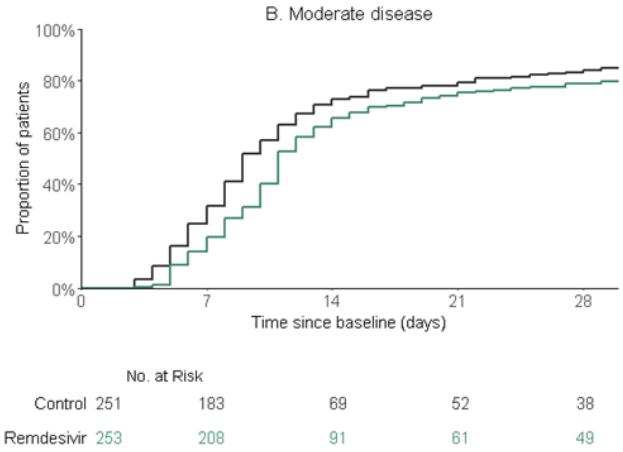


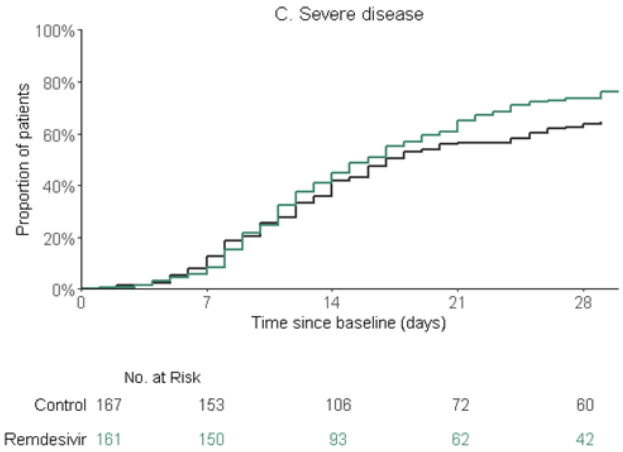


Supplementary Figure S4. Time to improvement of at least 2 categories or the 7-point ordinal scale or hospital discharge between baseline and day 29 in the intention-to-treat population of the DisCoVeRy trial, according to disease severity at randomization in all participants (panel A), in participants with moderate disease at randomization (panel B) and in participants with severe disease at randomization (panel C).

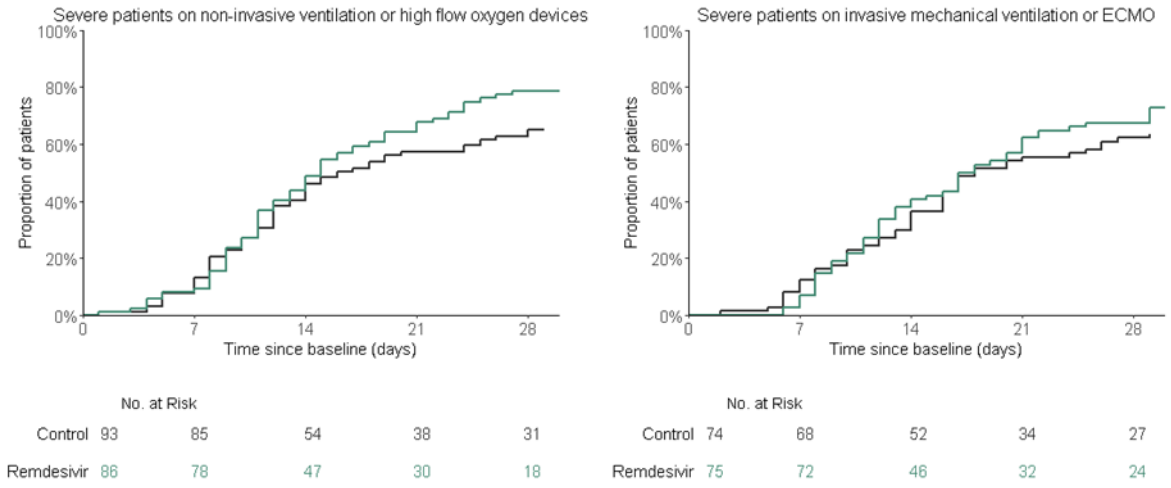
Analyses were stratified on the disease severity at randomization and reported aazard ratio is adjusted on disease severity at randomization. Remdesivir (green line); control (black line). HR, Hazard ratio; 95%CI, 95% confidence interval.



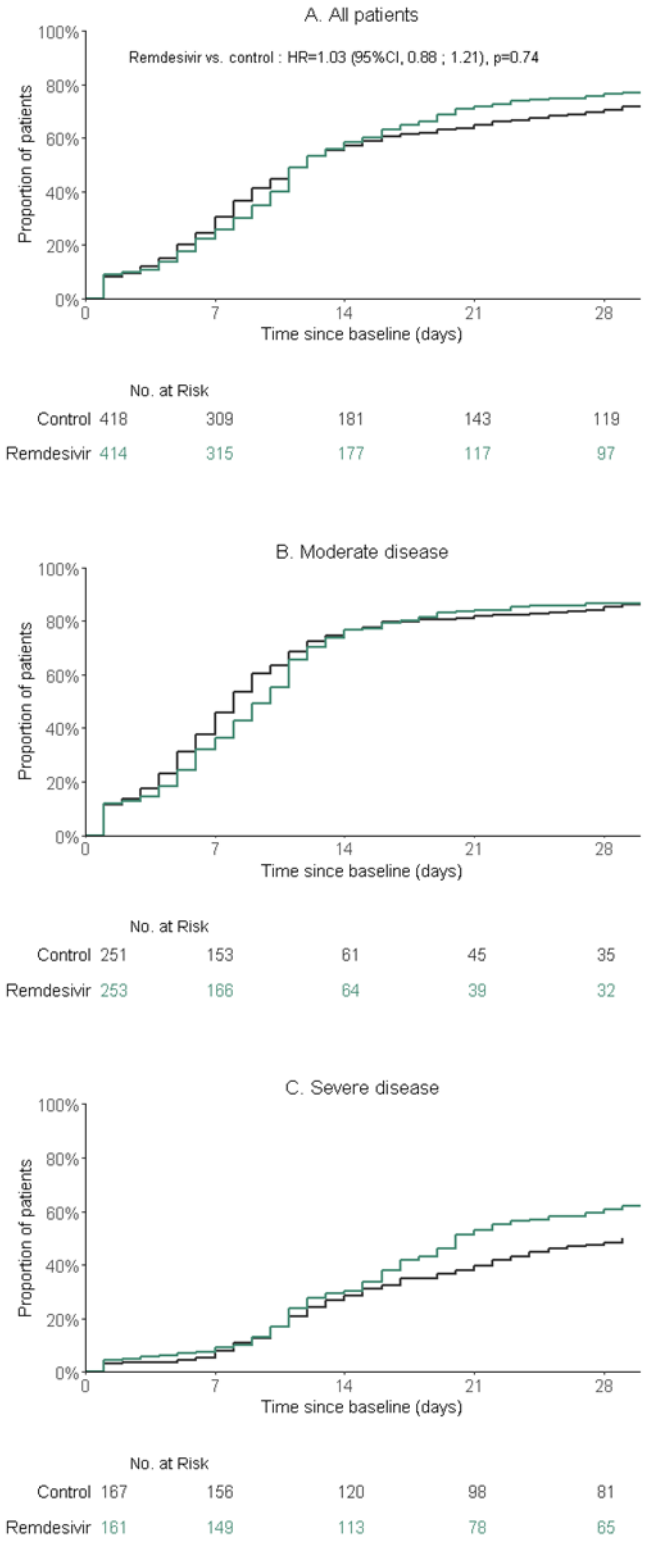




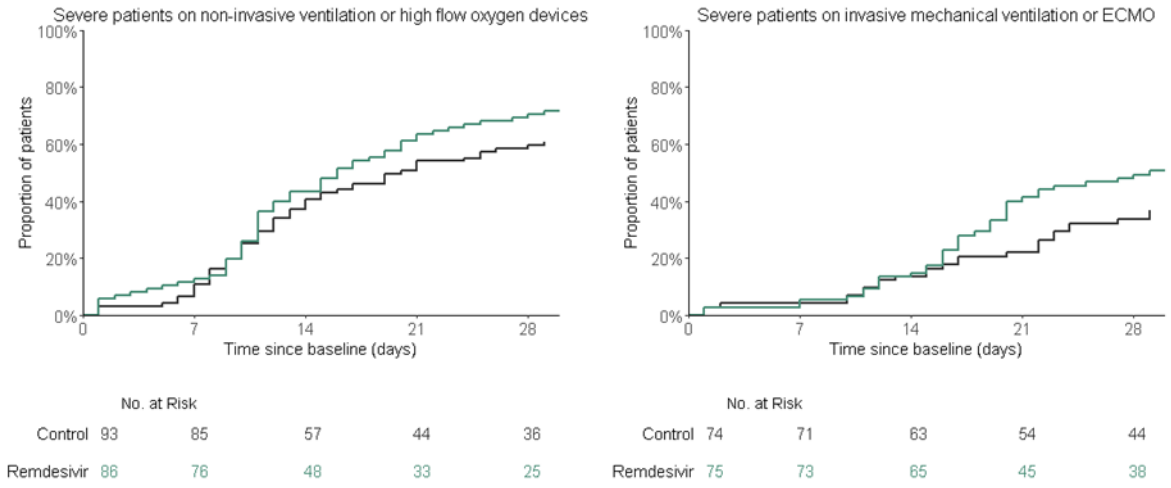
Supplementary Figure S5. Time to improvement of at least 2 categories or the 7-point ordinal scale or hospital discharge between baseline and day 29 in the intention-to-treat population of the DisCoVeRy trial, in severe patients stratified by absence (left) or presence (right) of invasive mechanical ventilation or ECMO at randomisation.
Remdesivir (green line); control (black line).



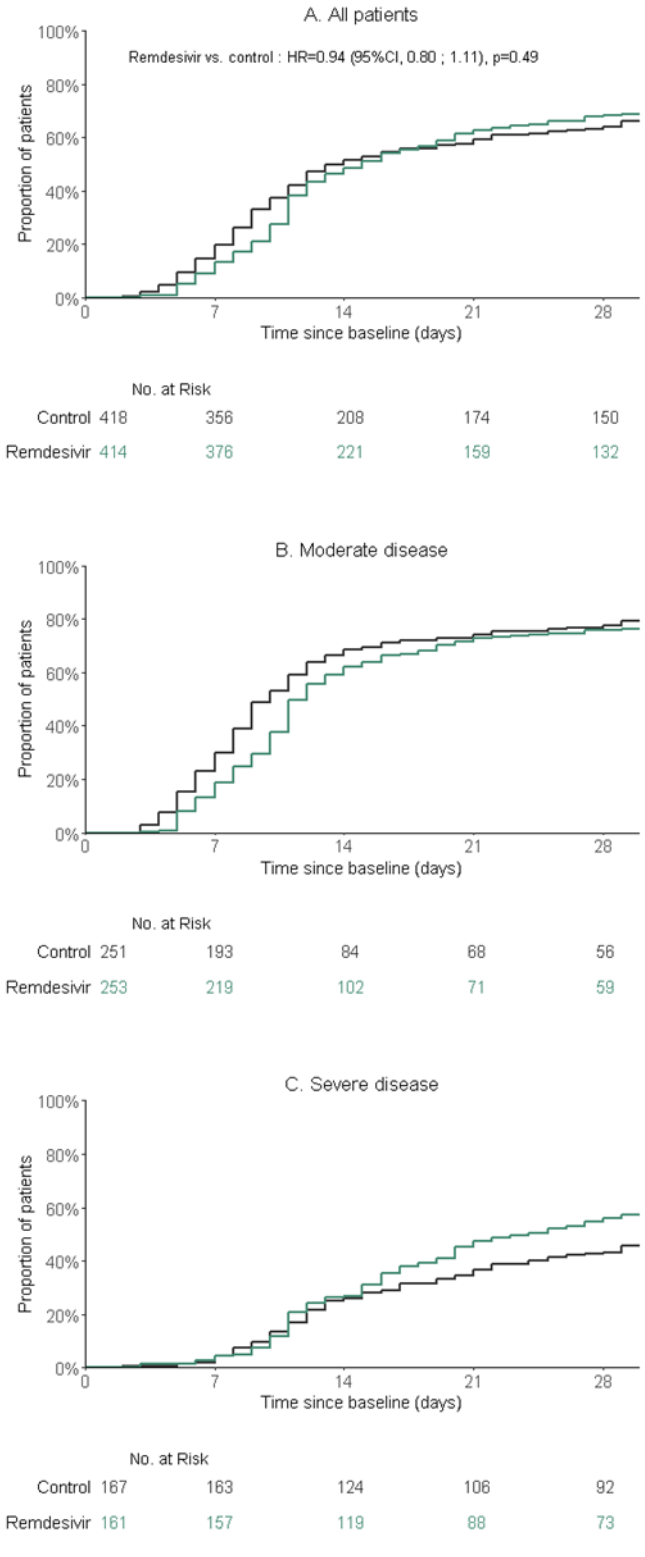
Supplementary Figure S6. Time to National Early Warning Score ≤2 or hospital discharge between baseline and day 29 in the intention-to-treat population of the DisCoVeRy trial, according to disease severity at randomization in all participants (panel A), in participants with moderate disease at randomization (panel B) and in participants with severe disease at randomization (panel C).
Remdesivir (green line); control (black line). HR, Hazard ratio; 95%CI, 95% confidence interval.



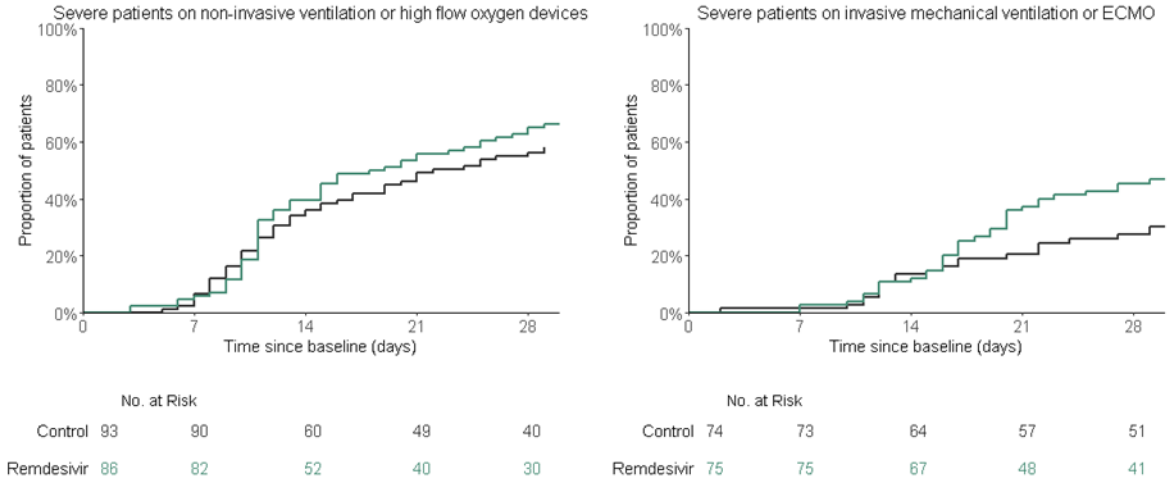
Supplementary Figure S7. Time to National Early Warning Score ≤2 or hospital discharge between baseline and day 29 in the intention-to-treat population of the DisCoVeRy trial, in severe patients stratified by absence (left) or presence (right) of invasive mechanical ventilation or ECMO at randomisation.
Remdesivir (green line); control (black line).



Supplementary Figure S8. Time to hospital discharge between baseline and day 29 in the intention-to-treat population of the DisCoVeRy trial, according to disease severity at randomization in all participants (panel A), in participants with moderate disease at randomization (panel B) and in participants with severe disease at randomization (panel C).
Remdesivir (green line); control (black line). HR, Hazard ratio; 95%CI, 95% confidence interval.

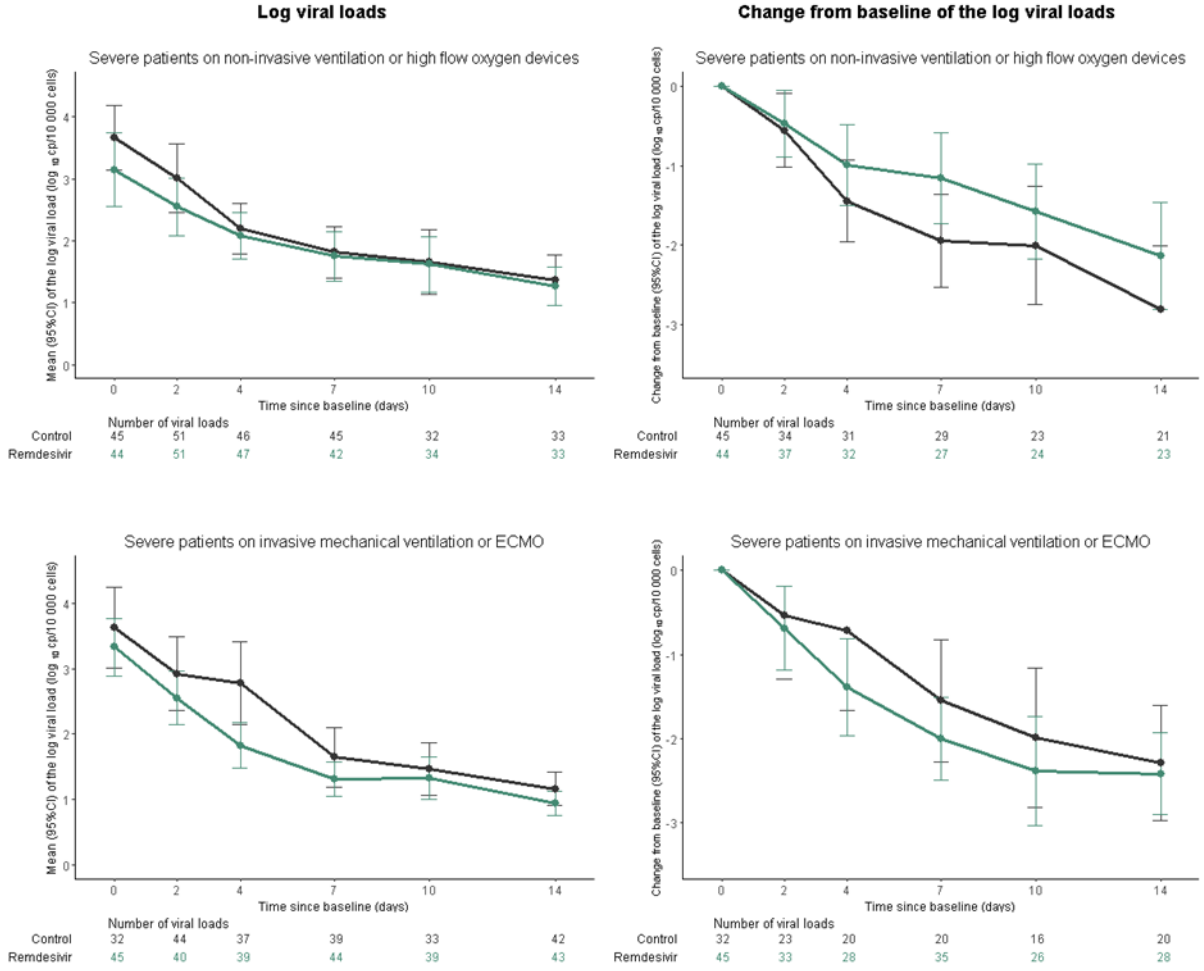


Supplementary Figure S9. Time to hospital discharge between baseline and day 29 in the intention-to-treat population of the DisCoVeRy trial, in severe patients stratified by absence (left) or presence (right) of invasive mechanical ventilation or ECMO at randomisation.
Remdesivir (green line); control (black line).



Supplementary Figure S10. Evolution of the normalized SARS-CoV-2 viral load in nasopharyngeal swabs between baseline and day 15 in the intention-to-treat population of the DisCoVeRy trial, in severe patients stratified by absence (left) or presence (right) of invasive mechanical ventilation or ECMO at randomisation: log_{10} viral loads (left), change from baseline of the log_{10} viral loads (right).

Data are presented as means (95%CI). Remdesivir (green line); control (black line).



CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	9
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	11
	2b	Specific objectives or hypotheses	12
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	12
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Suppl appendix
Participants	4a	Eligibility criteria for participants	12-13
	4b	Settings and locations where the data were collected	12
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	14
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	14-15
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	16-17
	7b	When applicable, explanation of any interim analyses and stopping guidelines	17
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	13
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	13
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	13
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	13
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	13

	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	18-19
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	18-19
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	19-20
	13b	For each group, losses and exclusions after randomisation, together with reasons	Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	19
	14b	Why the trial ended or was stopped	17
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	19-20
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	29-22, Table 2, Suppl Appendix
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	29-22, Table 2, Suppl Appendix
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	29-22, Table 2, Suppl Appendix
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Table 3
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	24-25
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	24-25
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	22-25
Other information			
Registration	23	Registration number and name of trial registry	19
Protocol	24	Where the full trial protocol can be accessed, if available	Suppl Appendix
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	19, 28-29

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

DisCoVeRy Study Group

Sponsor: Sandrine Couffin-Cadièrgues, Christelle Delmas, Hélène Esperou (Pôle de Recherche Clinique, Inserm, Paris, France)

Investigators:

Austria*:* Bernd Lamprecht (Kepler Universitätsklinikum Linz, Linz), Michael Joannidis (Medizinische Universität Innsbruck, Innsbruck), Alexander Egle, Richard Greil (Paracelsus Medical University Salzburg, SCRI-CCCI and AGMT)

Belgium*:* Antoine Altdorfer, Vincent Fraipont (Centre Hospitalier Régional de la Citadelle, Liège), Leila Belkhir (Cliniques Universitaires de Saint Luc, Bruxelles), Maya Hites, Gil Verschelden (Hôpital Erasme, Cliniques Universitaires de Bruxelles)

France: Violaine Tolsma, David Bougon (Centre Hospitalier Annecy-Genevois) ; Agathe Delbove, Marie Gousseff (Centre Hospitalier Bretagne-Atlantique, Vannes) ; Nadia Saidani, Guilhem Wattecamps (Centre Hospitalier Cornouaille, Quimper) ; Félix Djossou, Loïc Epelboin (Centre Hospitalier de Cayenne Andrée Rosemon) ; Jean-Philippe Lanoix, Pierre-Alexandre Roger, Claire Andrejak, Yoann Zerbib (Centre Hospitalier Universitaire de Amiens) ; Kevin Bouiller, Catherine Chirouze, Jean-Christophe Navellou (Centre Hospitalier Universitaire de Besançon) ; Alexandre Boyer, Charles Cazanave, Alexandre Duvignaud, Didier Gruson, Denis Malvy (Centre Hospitalier Universitaire de Bordeaux) ; Henry Lessire, Martin Martinot (Hospices Civils de Colmar) ; Pascal Andreu, Mathieu Blot, Lionel Piroth, Jean Pierre Quenot (Centre Hospitalier Universitaire de Dijon) ; Olivier Epaulard, Nicolas Terzi (Centre Hospitalier Universitaire de Grenoble-Alpes) ; Karine Faure, Emmanuel Faure, Julien Poissy, Saad Nseir (Centre Hospitalier Régional Universitaire de Lille) ; Florence Ader, Laurent Argaud, Tristan Ferry, Thomas Perpoint, Vincent Piriou, Jean-Christophe Richard, Julien Textoris, Florent Valour, Florent Wallet (Hospices Civils de Lyon) ; André Cabié, Jean-Marie Turmel, Cyrille Chabartier (Centre Hospitalier Universitaire de Martinique, Fort-de-France) ; Rostane Gaci, Céline Robert (Centre Hospitalier Régional de Metz-Thionville) ; Alain Makinson, Vincent Le Moing, Kada Klouche (Centre Hospitalier Universitaire de Montpellier) ; Olivier Hinschberger, Joy Mootien (Centre Hospitalier de Mulhouse Sud-Alsace) ; Sébastien Gibot, François Goehringer, Antoine Kimmoun, Benjamin Lefevre (Centre Hospitalier Régional Universitaire de Nancy) ; David Boutoille, Emmanuel Canet, Benjamin Gaborit, Paul Le Turnier, François Raffi, Jean Reignier (Centre Hospitalier Universitaire de Nantes) ; Johan Courjon, Jean Dellamonica, Sylvie Leroy, Charles-Hugo Marquette (Centre Hospitalier Universitaire de Nice), Paul Loubet, Claire Roger, Albert Sotto (Centre Hospitalier Universitaire de Nîmes) ; Cédric Bruel, Benoît Pilmis (Groupe Hospitalier de Paris Saint-Joseph) ; Guillaume Geri, Elisabeth Rouveix-Nordon (Hôpital Ambroise Paré, Assistance Publique – Hôpitaux de Paris); Olivier Bouchaud (Hôpital Avicenne, Assistance Publique – Hôpitaux de Paris); Samy Figueiredo, Stéphane Jaureguiberry, Xavier Monnet (Hôpital Bicêtre, Assistance Publique – Hôpitaux de Paris); Lila Bouadma, François-Xavier Lescure, Nathan Peiffer-Smadja, Jean-

François Timsit, Yazdan Yazdanpanah (Hôpital Bichat - Claude Bernard, Assistance Publique – Hôpitaux de Paris); Solen Kernéis, Marie Lachâtre, Odile Launay, Jean-Paul Mira (Hôpital Cochin, Assistance Publique – Hôpitaux de Paris) ; Julien Mayaux, Valérie Pourcher (Hôpital de la Pitié-Salpêtrière, Assistance Publique – Hôpitaux de Paris); Jérôme Aboab, Flora Crockett, Naomi Sayre (Hôpital Delafontaine, Saint-Denis), Clément Dubost, Cécile Ficko (Hôpital d'Instruction des Armées Bégin, Saint Mandé) ; David Lebeaux (Hôpital Européen Georges-Pompidou, Assistance Publique – Hôpitaux de Paris) ; Sébastien Gallien, Armand Mekontso-Dessap (Hôpital Henri-Mondor, Assistance Publique – Hôpitaux de Paris) ; Jérôme Le Pavec, Francois Stefan (Hôpital Marie Lannelongue, Le Plessis-Robinson); Hafid Ait-Oufella, Karine Lacombe (Hôpital Saint-Antoine, Assistance Publique – Hôpitaux de Paris); Jean-Michel Molina (Hôpital Saint-Louis, Assistance Publique – Hôpitaux de Paris); Murielle Fartoukh, Gilles Pialoux (Hôpital Tenon, Assistance Publique – Hôpitaux de Paris) ; Firouzé Bani-Sadr, Bruno Mourvillier (Centre Hospitalier Universitaire de Reims) ; François Benezit, Fabrice Laine, Bruno Laviolle, Yves Le Tulzo, Matthieu Revest (Centre Hospitalier Universitaire de Rennes) ; Elisabeth Botelho-Nevers, Amandine Gagneux-Brunon, Guillaume Thiery (Centre Hospitalier Universitaire de Saint-Étienne) ; Raphaël Clere-Jehl, François Danion, Yves Hansmann, Ferhat Meziani, Walid Oulehri, Yvon Ruch, Charles Tacquard (Centre Hospitalier Universitaire de Strasbourg) ; Fanny Bounes-Vardon, Guillaume Martin-Blondel, Marlène Murris-Espin, Béatrice Riu-Poulenc (Centre Hospitalier Universitaire de Toulouse) ; Vanessa Jean-Michel, Eric Senneville (Centre Hospitalier de Tourcoing) ; Louis Bernard, Denis Garot (Centre Hospitalier Universitaire de Tours).

Luxembourg: Jean Reuter, Thérèse Staub (Centre Hospitalier de Luxembourg) ; Marc Berna (Hôpitaux Robert Schuman).

Portugal: Sandra Braz, Joao Miguel Ferreira Ribeiro (Centro Hospital Universitário de Lisboa Norte, Hospital de Santa Maria); José-Artur Paiva, Roberto Roncon-Albuquerque (Centro Hospitalar Universitário São João de Porto).

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Trial management: Aline Dechanet (Hôpital Bichat - Claude Bernard, Assistance Publique – Hôpitaux de Paris) ; Juliette Saillard (ANRS-MIE), Marina Dumousseaux, Assia Ferrane (Pôle de Recherche Clinique, Inserm), Claire Fougerou-Leurent (Centre Hospitalier Universitaire de Rennes) ; Marion Noret (Réseau national de recherche clinique en infectiologie).

Pharmacovigilance: Alpha Diallo, Noémie Mercier, Vida Terzić(ANRS-MIE).

Statistics and data management: Drifa Belhadi, Charles Burdet, Jérémie Guedj, France Mentré, Priyanka Velou (Hôpital Bichat - Claude Bernard, Assistance Publique – Hôpitaux de Paris) ; Dominique Costagliola (Institut Pierre-Louis d'Épidémiologie et de Santé Publique)

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We acknowledge the DisCoVeRy Steering Committee (by alphabetical order):
Voting members: Florence Ader, Dominique Costagliola, Alpha Diallo, Alexander Egle, Hélène Espérou, Monika Halanova, Maya Hites, Bruno Lina, France Mentré, José-Artur Paiva, Marie-Thérèse Staub, Yazdan Yazdanpanah.
Non-voting members: Pascale Augé, Drifa Belhadi, Charles Burdet, Mireille Caralp, Sandrine Couffin-Cadiergues, Aline Dechanet, Marta Del Alamo, Christelle Delmas, Jacques Demotes, Marina Dumousseaux, Joe Eustace, Richard Greil, Fionnuala Keane, Marie-Paule Kiény, Soizic Le Mestre, Bernd Muehlbauer, Mickael Ohana, Nathan Peiffer Smadja, Ventzislava Petrov-Sanchez, Gilles Peytavin, Julien Poissy, Isabel Püntmann, Jean Reuter, Juliette Saillard, Vida Terzić.

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Laurent Abel, Florence Ader, Toni Alfaiate, Claire Andrejak, Drifa Belhadi, Lila Bouadma, Maude Bouscambert, Charles Burdet, Anissa Chair, Dominique Costagliola, Sandrine Couffin-Cadiergues, Eric D'Ortenzio, Aline Dechanet, Christelle Delmas, Alpha Diallo, Axelle Dupont, Hélène Esperou, Assia Ferrane, Claire Fougerou-Leurent, Alexandre Gaymard, Ambre Gelley, Jérémie Guedj, Benjamin Hamze, Vinca Icard, Samira Laribi, Minh-Patrick Lê, Soizic Le Mestre, Delphine Lebrasseur- Longuet, François-Xavier Lescure, Benjamin Leveau, Bruno Lina, France Mentré, Noémie Mercier, Laëtitia Moinot, Marion Noret, Nathan Peiffer-Smadja, Ventzislava Petrov-Sanchez, Gilles Peytavin, Julien Poissy, Juliette Saillard, Caroline Semaille, Marie-Capucine Tellier, Jean-François Timsit, Sarah Tubiana, Priyanka Velou, Linda Wittkop, Yazdan Yazdanpanah.

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Clinical aspects: Florence Ader, Claire Andrejak, Charles Burdet, Christelle Delmas, Marina Dumousseaux, François-Xavier Lescure, Nathan Peiffer-Smadja, Julien Poissy, Juliette Saillard.
Study products: Aline Dechanet, Christelle Delmas, Marina Dumousseaux, Assia Ferrane, Benjamin Hamze, Juliette Saillard.
Methodology and Statistics: Drifa Belhadi, Charles Burdet, Dominique Costagliola, Axelle Dupont, France Mentré.

Data: Toni Alfaiate, Drifa Belhadi, Charles Burdet, Aline Dechanet, Christelle Delmas, Yakhara Diawara, Claire Fougerou-Leurent, Annabelle Metois, Priyanka Velou.

Radiology: Florence Ader, Claire Andrejak, Charles Burdet, Mickael Ohana, Nathan Peiffer-Smadja.

Virology: Maude Bouscambert, Charles Burdet, Alexandre Gaymard, Benjamin Leveau, Bruno Lina, France Mentré.

Pharmacology: Alpha Diallo, Minh Le, Benjamin Leveau, France Mentre, Nathan Peiffer-Smadja, Gilles Peytavin, Minh Le, Sarah Tubiana.

Immunology: Laurent Abel, Florence Ader, Alexandre Belot, Maude Bouscambert, Charles Burdet, Darragh Duffy, François-Xavier Lescure, France Mentré, Nathan Peiffer-Smadja, David Smadja.

Genetics: Laurent Abel, Christelle Delmas, Benjamin Leveau, France Mentré, Sarah Tubiana.

Collection of biological human samples: Aline Dechanet, Christelle Delmas, Vinca Icard, Ouifiya Kafif, Benjamin Leveau, Bruno Lina, Céline Sakonda, Sarah Tubiana.

Safety matters: Drifa Belhadi, Aline Dechanet, Christelle Delmas, Alpha Diallo, Noemie Mercier, Laurence Moachon, Nathan Peiffer-Smadja, Vida Terzić.

Regulatory affairs, Monitoring and Financial management: Sandrine Couffin-Cadiergues, Aline Dechanet, Christelle Delmas, Marina Dumousseaux, Hélène Esperou, Assia Ferrane, Claire Fougerou-Leurent, Delphine Lebrasseur, Soizic Le Mestre, Noemie Mercier, Marion Noret, Juliette Saillard, Vida Terzić.

Communication: Florence Ader, Sandrine Couffin-Cadiergues, Aline Dechanet, Christelle Delmas, Marina Dumousseaux, Hélène Esperou, Claire Fougerou-Leurent, France Mentré, Marion Noret, Nathan Peiffer-Smadja, Juliette Saillard, Yazdan Yazdanpanah.

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